

REMARKS

Claim 42 has been amended. Claim 72 has been canceled. Claims 74-76 have been added. Claims 42-71 and 73-76 are pending. Support for the amendments to claim 42 can be found in the specification, for example, at Example 8 and Figure 3. No new matter is added by the amendments to the claims.

Rejections under 35 U.S.C. §112, first paragraph

In the Advisory Action mailed February 4, 2004, the Examiner maintained the rejection of the claims as not enabled. Specifically, the Examiner has held that "the breadth of the claims is excessive with regard to Applicants claiming a method of treating any and all injuries to photoreceptors, or for treating a degenerating photoreceptor [because] Applicants have only demonstrated that they are able to proliferate cells in vitro." (Paper No. 101503, page 4). In particular, the Examiner asserts that "it is not clear that the animal model in Example 8 is an art-accepted model of in vivo treatment of photoreceptors." Applicants respectfully traverse.

Applicants respectfully refer the Examiner to the "Training Materials for Examining Patent Applications with Respect to 35 U.S.C. § 12, First Paragraph – Enablement Chemical/Biotechnical Applications." at section III(A)(2)(c)(ii), entitled "Correlation: *In Vitro/In Vivo*." As discussed in the training materials, the issue of "correlation" is dependent on the state of the art. That is, if the model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner ***has evidence to the contrary***. Even with such evidence, the Examiner must still weigh the evidence for and against correlation and decide ***whether one skilled in the art would accept the model as reasonably correlating to the condition***. *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995)[*emphasis added*]. The Examiner must also provide reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. A rigorous or an invariable exact correlation is not required. *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985).

The Examiner has provided no evidence that the rat retinal explant model used in Example 8 is not an art-accepted model for photoreceptor proliferation. Furthermore, the

Examiner has not provided any evidence indicating that one skilled in the art would not accept the retinal explant model as reasonably correlating to an injury to or a disorder of an eye comprising degeneration of a photoreceptor cell. Therefore, Applicants respectfully submit that the Examiner has not met his burden.

Applicants submit herewith publications from peer-reviewed journals that support Applicants position that the in vitro rat retinal explant model is accepted by skilled artisans as correlating with in vivo proliferation and differentiation of retinal cells, including photoreceptor cells.

Applicants respectfully direct the Examiner's attention to the following: (1) an article by Gail M. Seigel, entitled "The Golden Age of Retinal Cell Culture," Molecular Vision, 1999, 5:4, which reviews the state of the art with respect to retinal cell culture. The author indicates that, even though in vitro studies have limitations, the advantages of in vitro studies, such as explant cultures, "outweigh the potential limitations." (See, column 1, second paragraph). The author further indicates that retinal explant cultures "have been ideal for studies of ...retinal differentiation." (See, column 2, third full paragraph) ("Retinal explants retain the highest degree of tissue preservation of all retinal cell culture systems and continue to be the method of choice for in vitro studies that require intact cell-cell associations."); (2) Kelley et al., "Regulation of Proliferation and Photoreceptor Differentiation in Fetal Human Retinal Cell Cultures," IOVS 1995, 36(7):1280, correlate findings of "proliferation of neuronal progenitor cells and the production of retinal neurons in vitro" using the rat retina, with "factors that may regulate neurogenesis in vivo." (See, page 1280, column 2); (3) an article by Schulz-key et al., entitled "Ciliary Neurotrophic Factor as a Transient Negative Regulator of Rod Development in Rat Retina," IOVS, 2002, 43(9):3099, which praises the in vitro rat explant model because "the laminar structure of the retina is largely preserved, allowing the study of the influence of CNTF on the formation of the photoreceptor layer and the phenotypic differentiation of rods from proliferating neuroepithelial cells that develop in an environment *resembling the in vivo situation*." (See, page 3099, column 2, second full paragraph) [emphasis added]; and (4) an article by Altshuler et al., entitled "Taurine Promotes the Differentiation of a Vertebrate Retinal Cell Type In Vitro," Development,

1993, 119:1317, in which the authors use a rat explant model to "identify taurine as one of several factors that might normally play a role in regulating rod photoreceptor development in vivo." (See, page 1318, column 1, last sentence of the second full paragraph and page 1328, column 1, first sentence of the second full paragraph). Additionally, Applicants provide herewith a peer-reviewed article by Bocker-Meffert et al., entitled "Erythropoietin and VEGF promote Neural Outgrowth from Retinal Explants in Postnatal Rats," IOVS, 2002, 43(6):2021, which describes rat retinal explants used to elucidate the effect of VEGF on axonal outgrowth of central neurons (See, page 2021, column 2, third through fifth full paragraphs). The authors correlate their in vitro rat explant experiments with retinal diseases such as diabetic retinopathy and retinal ischemic diseases. (See, page 2025, first full paragraph).

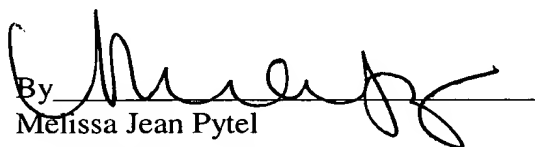
Applicants respectfully submit that the enclosed articles demonstrate that the rat explant model, as used in Example 8, is accepted in the art for studying retinal differentiation and proliferation and is believed to correlate with photoreceptor development in vivo. Applicants therefore request withdrawal of this rejection.

Conclusion

The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application. Applicants believe that there are no fees due in connection with the filing of this paper. However, should a fee be due, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the appropriate fee should also be charged to our Deposit Account.

Dated: April 9, 2004

Respectfully submitted,

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Enclosures
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